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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,600	03/24/2006	James Wilson	UPN-P3230USA	6834

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
07/09/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@howsonandhowson.com

Office Action Summary	Application No.	Applicant(s)	
	10/573,600	WILSON ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,60-66 and 68-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45, 60-66, 68-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 4/22/10. Claims 45, 60-66 and 68-76 are pending.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically, the date of inventor Alvira has been altered without initials.

Claim Objections

Claims are objected to because of the following informalities: **These objections are maintained for reasons of record in the office action mailed 1/22/10 and restated below.**

Claim 45 recites "a non-naturally occurring AAV according to claim 59". However, when referring to previous limitations, it is proper to use the article --the-- as opposed to "a" which implies a new limitation. As well, in claim 45, the phrase "said rAAV" is incorrect. When using the phrase "said" the limitation is repeated as previously recited in exact terms. In this case, the term rAAV does not appear in the claims. It is recommended that claim 45 be amended to recite --A method of delivering the transgene of claim 60 to a cells, said method comprising the step of contacting the cell with the non-naturally occurring AAV.

In claim 64 an article is required prior to each of low density, high density . As well, the transgene is not selected from the group but --the transgene encodes a protein selected from the group--.

These are new objections necessitated by applicants' amendment.

The recitation in claim 63, "A transgene" should be amended to --the transgene-- as the transgene has been previously recited,. As well, the phrase "wherein said minigene comprise the transgene" is redundant and should be deleted.

In claim 70, the claim would be clearer if recited as --wherein the vp3 protein has an amino acid sequence of 203-736 of SEQ ID NO:123--. First it is not "a vp3" as the previous claim already indicates there is a vp3 and secondly, the seq3eunce is not "of 203-736" but has an amino acid sequence with these amino acids.

Claim 74 does not include the number of origin for the fragment ending in 173.

These are new objections.

In claim 61, the claim would be clearer if recited in the same format as claim 60. i.e. -- vp1, nucleotides (nt) 1-2211 of SEQ ID NO:3, vp2, nt 411-2211 of SEQ OD O;3; and vp3, nt 609-2211 of SEQ ID NO;3 -- followed by deletion of the phrase "wherein the nucleotides numbers are or AAV9, SEQ ID NO:3".

Appropriate correction is required.

Applicant is advised that should claim 66 be found allowable, claim 71 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims are drawn to the same subject matter i.e. claim 65 wherein the capsid proteins comprise an amino acid sequence with 97% identity to 203-736 of SEQ ID NO:123.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 68, 69 amd 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections necessitated by applicants' amendment.**

Claim 68 recites the limitation "the AAV protein fragments" in claim 70. There is insufficient antecedent basis for this limitation in the claim.

Claim 69 recites the limitation "the AAV9/HU.14 capsid protein fragments" in claim 70. There is insufficient antecedent basis for this limitation in the claim.

Claim 75 recites the limitation that the fragment from SEQ ID NO:123 is from 724-738. However, SEQ ID NO:123 does not extend beyond 736.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45, 60-66 and 68-73 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated recombinant AAV comprising an AAV9 capsid wherein the AAV9 capsid is SEQ ID NO:123 or comprises vp3 with amino acids 203-736 of SEQ ID NO:123, does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This rejection is maintained for reasons of record in the office action mailed 1/22/10 and restated below based upon applicants' amendment.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The instant claims are drawn to a 1) an AAV9 capsid comprising a vp1, a vp2 and a vp3 wherein at least one the capsid proteins is an AAV9 capsid protein is selected from amino acids 1-736, 138-736 and 203-736 of SEQ ID NO:123 (vp1, vp2 and vp3 respectively), compositions

comprising and methods of administering 2) a non-naturally occurring AAV comprising a vp1, a vp2 and a vp3 wherein the capsid proteins comprise at least 95% identity to amino acids 203-736 of SEQ ID NO:123, compositions comprising and methods of administering, 3) an AAV comprising a chimeric capsids wherein at least one protein comprises a fragment of AV9 i.e. amino acids 25-28, 137-143, 154-156, -173, 182-186, 185-198, 260-273, 262-264, 261-174, 262-274, 381-383, 670-706, 1-184, 199-289, 274-446, 603-659, 724-738, 185-198, 447-477, 495-602, 660-669 and 707-723 (claim 74, 75 and 76).

Regarding #1, the claims are drawn to any AAV so long as the AAV has at least one of vp1, vp2 or vp3 from AAV9. It is noted that the amended claim is distinct from the previous claim set filed 11/9/09 by no longer requiring that the capsid be an AAV9 capsid. The amended claim only requires that the capsid comprise a single AAV9 capsid protein. It is not clear that the specification is drawn to a capsid comprising a mixed population of capsid proteins i.e. an AAV9 vp1, vp2 or vp3 wherein the alternative vp proteins are from another serotype. It is not clear that this capability is possible given the related nature of the vp1, vp2 and vp3 proteins wherein expression of SEQ ID NO:123 inherently results in production of all 3. Rather, it appears as if the specification is drawn to a pseudotyped AAV wherein the capsid is an AAV9 capsid or variant thereof as well as chimeric capsid proteins wherein portions of the vp1, vp2 and vp3 proteins are from AAV9 (see ¶ 0091 and 0103).

> [0091] Particularly desirable proteins include the AAV capsid proteins. which are encoded by the nucleotide sequences identified above. The AAV capsid is composed of three proteins, vp1, vp2 and vp3, which are alternative splice variants. The full-length sequence provided in FIG. 2 is that of vp1. The AAV9/HU.14 capsid proteins include vp1 [amino acids (aa) 1 to 736 of SEQ ID NO: 123], vp2 [about aa 138 to 736 of SEQ ID NO: 123], vp3 [about aa 203 to 736 of SEQ ID NO: 123], and functional fragments thereof. Other desirable fragments of the capsid protein include the constant and variable

regions, located between hypervariable regions (HVR). Other desirable fragments of the capsid protein include the HVR themselves.

Regarding #2, the claims are drawn to any AAV with an AAV9 capsid. However, structurally the AAV9 capsid comprises vp3 sequences or variants thereof. However, by recitation of the protein in terms of identity, a potentially large number of proteins are actually recited of which most that may or may not encode a protein with the capabilities of capsid function. The specification teaches only SEQ ID NO:123 and does not provide those variable amino acids nor any fragments such that a person of skill in the art would recognize those amino acids that are related by 95% or 97% with capsid function.

The breadth of enabled subject matter is not commensurate in scope with the claims. The amount of direction presented and the number of working examples provided in the specification are very narrow compared to the breadth of claims at issue. MPEP 2164.05 teaches, "However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention." In this case, the specification teaches only that SEQ ID NO:123 is essential to form a capsid or else use of a number of sequences in the context of an entire capsid protein. However, the claims are directed to a large genus of proteins that are variants and fragments with no requirement of structure.

As to nucleic acids and proteins that are 95% or 97% identical to SEQ ID NO:123, the following considerations must be made. The specification discloses that SEQ ID NO:123 is 736 amino acids. And while the disclosure states that any peptide with at least 95% or at least 97%

identity can be used in the AAV, the disclosure does not demonstrate what sequences must be retained and what sequences are dispensable. For proteins with 3% variability of sequence, a protein of 736 amino acids can have as many as 22 different *combinations* of amino acids mutated. 22 mutational combinations, randomly made, amounts to characterizing the structure for allowable mutations. For nucleic acids, 5% variability means that 36 amino acids can be altered. At issue is not whether one could make 22 or 36 random combinations of mutations but whether the specification provides the guidance a to which amino acids can be altered and which cannot. The ability to determine *a priori* whether a variant or unknown sequence will encode a protein with a particular activity is not a high art. A particular protein sequence determines the protein's structural, and functional properties, and a predictability of a representative number of claimed polypeptide sequences that display noteworthy biological properties requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which a protein's structure relates to its functional usefulness (see Guo et al and Lesk et al). Here, the question is can the functionality of variants and fragments be known with predictability. Lesk teaches the lack of predictability of claiming variants of a protein even with a known function.

> *Nevertheless, prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and / or structure between a protein of unknown function and one or more well-understood proteins.* Alternative methods include conservation patterns in members of a functionally uncharacterised family for which many sequences and structures are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof

As demonstrated by Lesk, methods of function prediction rely on comparison of proteins of known function with those of unknown function. In this case, the protein (SEQ ID NO:6) is used to derive function from a randomly modified protein, however, prediction of function from sequence is difficult because even homologous proteins have different function. Lesk clearly confirms that predictability of ascribing the same function as SEQ ID NO:6 to protein variants is unpredictable.

> In most cases, predictions suggest, but do not determine, the general class of function. Their most useful effect is to guide investigations in the laboratory to confirm, or refute, the prediction, and, even if correct, to define the function in greater detail.
> We conclude that predictions are useful but no substitute for work in the laboratory. Indications from theory may indict, but only experimental evidence can convict.

Guo et al teach that the probability that a protein will tolerate a substitution or random alteration requires a clear understanding of the structural-functional correlations of the protein.

> However, to date, we lack a quantitative measure of the degree of proteins' tolerance for random amino acid changes that occur at a random position in the protein. If a rigorous measure of proteins' degree of tolerance of random amino acid changes can be defined, then such fundamental calculations as the steepness of protein fitness landscapes or the rate of introduction of deleterious mutations into coding genomes can be more clearly delineated. Further understanding of the nature of tolerated amino acid substitution's can also lend !insight into protein folding, and design

Guo et al suggest that an understanding as to the critical region and defining the "x-factor" allow one to predict the probability that a change will be inactivating or will be tolerated are required. However, the instant case, does not propose substitutions of specific regions. Rather, the invention relies on random mutagenesis with the assumption that so long as 90% of the protein is the same then the resulting function will be the same.

Furthermore, Richards (1997) *Cell Mol. Life Sci.* 53:790-802 teaches, "In terms of structural alterations and thermostability, responses to genetic mutations are context dependent and remain difficult to predict with any confidence." (Abstract, column 1.) Thus, Richards

teaches that the effect of mutation on protein stability, a prerequisite for biological function, is unpredictable. Richards also teaches that even limited amino acid modifications can have dramatic effects on protein structure and function. In the second column on page 791, Richards cites the example of influenza virus hemagglutinin protein, wherein alterations in the ionization state of just a few ionizable groups dramatically alters the biological behavior of the molecule. Citing a published study of done on the gene V protein, Richards teaches that, in spite of only limited modification at two amino acid positions, "The effects on the overall stability of the protein were remarkably variable." (page 794, column 1). In the paragraph bridging pages 796 and 797, Richards teaches, "In single site mutants, the structural changes are generally greatest near the site of mutation, and moving away, decrease radially in all directions. *Even the small changes are so complex that the linkage relations do not allow assignments of the energetic changes to unique parts of the altered residue and its immediate contacts*" (emphasis added) and "There is no convincing explanation yet of how the changes in binding can produce a major movement over such a distance." Finally, in the first full paragraph in the second column on page 793, Richards teaches, "Almost all mutations are accompanied by some conformational change, making prediction of the effects on stability difficult. *In most cases mutations lead to lowering of the stability.*" (Emphasis added.) Thus, Richards teaches that small changes in the primary structure of a protein frequently have dramatic effects on the higher order structure and function of the protein, and that these effects are highly unpredictable. However, applicants propose mutation of 74 and 37 amino acids which according to the art can alter function and 3d integrity even at the level of a single amino acid mutation.

Given the large size and diversity of the recited sequences, the absence of disclosed or art recognized correlations between structure and function and the large number of potential sequences or homologues, variants, and fragments and in view of the unpredictability of the art of predicting the functional and structural nature of homologues, variants, and fragments of SEQ ID NO:123: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of a protein from primary sequence alone, the lack of adequate working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

Furthermore, the relationship of enablement with the requirement for written description is acknowledged by the MPEP. To this end, the court and the Board have repeatedly held (Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,18 USPQ2d 1016 (CA FC, 1991); Fiers v. Revel, 25 USPQ2d 1601 (CA FC 1993); Fiddes v. Baird, 30 USPQ2d 1481 (BPAI 1993) and Regents of the Univ. Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the molecule itself. It is not sufficient to define a protein solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any protein with that biological property. Naming a type of material generically known to exist, in the absence of

knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a amino acids, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all peptides that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. Also, where a claim purports to cover all protein with a specific function and the specification discloses but a single one known to do so, the situation is analogous to a single means claim and does not meet the enablement requirement under para. 1 ' of§112. Specifically, in the instant case, applicants propose a functional relationship of the related and fragmentary amino acids, but there is no requirement either in the claims or the specification for structural requirements such that the structure-function relationship can be determined or so that the genus of peptides claimed is commensurate in scope with the disclosure.

Response to Amendments

Applicants argue that there are two disclosed sequences SEQ ID NO:121 and 122 that provide examples of sequences that are 95% identical to SEQ ID NO:123. However, it is not clear that the two additional sequences provides structural data sufficient to identify those regions that can be retained and those that can additional. n light of the written description requirement, the Federal Circuit has repeatedly held that claims directed to a broad genus may not be adequately supported when the applicant describes only a small number of species

Regents" of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997). To satisfy the written description requirement in the case of a chemical or biotechnological genus, more than a statement of the genus is normally required. One must show that one has possession, as described in the application, of sufficient species to show that he or she invented and disclosed the totality of the genus. The "representative number of species" must be representative of the entire genus and, reflect variation between the species of the genus. The physiological art is recognized as unpredictable (MPEP 2164.03.). In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. In order for a single species, as in the instant case, to describe the genus, a correlation (known or disclosed) between function and structure can establish the species as representative of the genus. By disclosing the two related sequences, applicants have not described a known correlation between the structure and function but have simply provided examples of related species. As the application fails to disclose the relevant identifying characteristics of a variant capsid having the function required by the claims, the skilled artisan would not know which proteins within the broad scope that have the ability to form a capsid with all the properties required of such a structure. In order for the species to describe the genus, a correlation (known or disclosed) between function and structure can establish the species as representative of the genus. In this case, the species represent natural variants of SEQ ID NO:123. However, the claims are drawn

more broadly to variants of SEQ ID NO:123 wherein the guidance as to required structural characteristics is not provided. This class of naturally occurring variants is neither representative of the entire genus nor reflects the variation that exists between the species of the recited genus. In Noelle v. Lederman, 355 F.3d 1343, 1350 (Fed. Cir. 2004), the courts determined "a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated." Slip op. at 7. It is noted that claims drawn to the two related species can be drafted.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 74-76 are rejected under 35 U.S.C. 102(a) and 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Patel et al (6,498,244; see entire document) or Gao et al (20050014262; see entire document). **This is a new rejection necessitated by applicants' amendment.**

Patel et al teach AAV comprising a capsid comprising fragments of AAV9 such as those bolded below. In the case of the sequences at 185-198, the sequences are so similar, the

sequences are so similar it is not clear there is a structural difference between the sequences of the instant case and those published by Patel et al. Specifically, the sequences differ by conservative substitutions.

```
RESULT 7
US-09-321-589-1
; Sequence 1, Application US/09321589
; Patent No. 6498244
; GENERAL INFORMATION:
;  APPLICANT: PATEL, SALIL D.
;  APPLICANT:  MCARTHUR, JAMES G.
;  TITLE OF INVENTION: ADENO-ASSOCIATED VIRUS CAPSID IMMUNOLOGIC DETERMINANTS
;  FILE REFERENCE: 39672
;  CURRENT APPLICATION NUMBER: US/09/321,589
;  CURRENT FILING DATE:  1999-05-28
;  NUMBER OF SEQ ID NOS: 1
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 1
;   LENGTH: 735
;   TYPE: PRT
;   ORGANISM: Adeno-associated virus
US-09-321-589-1

  Query Match             81.7%;  Score 2656.5;  DB 2;  Length 735;
  Best Local Similarity   80.8%;  Pred. No. 2.3e-221;
  Matches  485;  Conservative   50;  Mismatches   62;  Indels    3;  Gaps
2;

Qy          1 TAPGKKRPVEQSPQEPDSSAGIGKSGAQPAKKRLNFGQTGDTESVPDPQPIGEPPAAPSG 60
              |||||||||| || |||||:| ||:| |||:|||||||||| :|||||||:|:|||||||
Db        138 TAPGKKRPVEHSPVEPDSSSGTGKAGQQPARKRLNFGQTGDADSVPDPQPLGQPPAAPSG197

Qy         61 VGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDRVITTSTRTWALPTYNNHLY120
              :|: |||:| |||:||||||||||:||||||||| |:|||||||||||||||||||||
Db        198 LGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDRVITTSTRTWALPTYNNHLY257

Qy        121 KQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFKLI180
              ||||: :  |:|||| ||||||||||||||||||||||||||||||||||||||||||||
Db        258 KQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFKLI315

Qy        181 FNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGSAHEGCLPPFPADVFMIPQY240
              |||||||| |:|  |||||||||||||||:|||||||||:|||||||||||:|||
Db        316 FNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGSAHQGCLPPFPADVFMVPQY375

Qy        241 GYLTLNDGSQAVGRSSFYCLEYFPSQMLRTGNNFQFSYEFENVPFHSSYAHSQSLDRLMN300
              ||||||:|||||||||||||||||||||||||| ||| ||:|||||||||||||||||
Db        376 GYLTLNNGSQAVGRSSFYCLEYFPSQMLRTGNNFTFSYTFEDVPFHSSYAHSQSLDRLMN435
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Qy        301 PLIDQYLYYLSKTINGSGQNQQT-LKFSVAGPSNMAVQGRNYIPGPSYRQQRVSTTVTQN359
              ||||||||||:|   ||   |: |:|| || |::  | ||::||| ||||||| |   |
Db        436 PLIDQYLYYLSRTNTPSGTTTQSRLQFSQAGASDIRDQSRNWLPGPCYRQQRVSKTSADN495

Qy        360 NNSEFAWPGASSWALNGRNSLMNPGPAMASHKEGEDRFFPLSGSLIFGKQGTGRDNVDAD419
              ||||::| ||: : ||||:||:|||||||||: |::||| || |||||||: : ||| :
Db        496 NNSEYSWTGATKYHLNGRDSLVNPGPAMASHKDDEEKFFPQSGVLIFGKQGSEKTNVDIE555

Qy        420 KVMITNEEEIKTTNPVATESYGQVATNHQSAQAQATGWVQNQGILPGMVWQDRDVYLQG479
              |||||:||||:|||||||| || |:|| |    || |  |  ||:|||||||||||||
Db        556 KVMITDEEEIRTTNPVATEQYGSVSTNLQRGNRQAATADVNTQGVLPGMVWQDRDVYLQG615

Qy        480 PIWAKIPHTDGNFHPSPLMGGFGMKHPPPQILIKNTPVPADPPTAFNKDKLNSFITQYST539
              ||||||||||:||||||||||:|||||||||||||||:| | |:  |  ||||||||
Db        616 PIWAKIPHTDGHFHPSPLMGGFGLKHPPPQILIKNTPVPANPSTTFSAAKFASFITQYST675

Qy        540 GQVSVEIEWELQKENSKRWNPEIQYTSNYYKSNNVEFAVNTEGVYSEPR-PIGTRYLTRNL599
              ||||||||||||||||||||||||||||| || ||:| |:| ||||||||||||||||||
Db        676 GQVSVEIEWELQKENSKRWNPEIQYTSNYNKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL735
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Gao et al teach AAV comprising a capsid comprising fragments of AAV9 such as those bolded below.

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RESULT 1
US-10-496-799-2
; Sequence 2, Application US/10496799
; Patent No. 7198951
; GENERAL INFORMATION:
;  APPLICANT: The Trustees of The University of Pennsylvania
;  APPLICANT:  Gao, Guangping
;  APPLICANT:  Wilson, James M.
;  APPLICANT:  Alvira, Mauricio
;  TITLE OF INVENTION: Adeno-Associated Virus (AAV) Serotype 9 Sequences,
Vectors Containing
;  TITLE OF INVENTION:  Same, and Uses Therefor
;  FILE REFERENCE: UPN-02734PCT
;  CURRENT APPLICATION NUMBER: US/10/496,799
;  CURRENT FILING DATE:  2004-06-08
;  PRIOR APPLICATION NUMBER: US 60/341,150
;  PRIOR FILING DATE: 2001-12-17
;  PRIOR APPLICATION NUMBER: US 60/386,132
;  PRIOR FILING DATE: 2002-06-05
;  NUMBER OF SEQ ID NOS: 7
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 2
;   LENGTH: 736
;   TYPE: PRT
;   ORGANISM: capsid protein of adeno-associated virus serotype 9
```

US-10-496-799-2

Query Match 87.0%; Score 2828; DB 3; Length 736;
Best Local Similarity 86.0%; Pred. No. 2.9e-236;
Matches 515; Conservative 32; Mismatches 52; Indels 0; Gaps 0;

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Qy          1 TAPGKKRPVEQSPQEPDSSAGIGKSGAQPAKKRLNFGQTGDTESVPDPQPIGEPPAAPSG 60
              |||||||||||||||||||:|||||| |||||||||||||:|||||||:|||| ||||
Db        138 TAPGKKRPVEQSPQEPDSSSGIGKSGQQPAKKRLNFGQTGDSESVPDPQPLGEPPEAPSG197

Qy         61 VGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDRVITTSTRTWALPTYNNHLY120
              :|  |||||||||:||||||||||:||||||||| ||||||||||||||||||||||||
Db        198 LGPNTMASGGGAPMADNNEGADGVGNSSGNWHCDSTWLGDRVITTSTRTWALPTYNNHLY257

Qy        121 KQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFKL180
              ||||| |||||:||| ||||||||||||||||||||||||||||||||||||||||||
Db        258 KQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFKL317

Qy        181 FNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGSAHEGCLPPFPADVFMIPQY240
              ||||||||| | | |||||||||||||||:||||||||||:|||||||||||||:|||
Db        318 FNIQVKEVTTNEGTKTIANNLTSTVQVFTDSEYQLPYVLGSAHQGCLPPFPADVFMVPQY377

Qy        241 GYLTLNDGSQAVGRSSFYCLEYFPSQMLRTGNNFQFSYEFENVPFHSSYAHSQSLDRLMN300
              |||||:||||:||||||||||||||||||||||||| ||:|||||||||||||||||
Db        378 GYLTLNNGSQALGRSSFYCLEYFPSQMLRTGNNFQFSYTFEDVPFHSSYAHSQSLDRLMN437

Qy        301 PLIDQYLYYLSKTINGSGQNQQTLKFSVAGPSNMAVQGRNYIPGPSYRQQRVSTTVTQNN360
              |||||||||| :|        ||| || ||||:|| | ||::||| |||||||||  |||
Db        438 PLIDQYLYYLVRTQTTGTGGTQTLAFSQAGPSSMANQARNWVPGPCYRQQRVSTTTNQNN497

Qy        361 NSEFAWPGASSWALNGRNSLMNPGPAMASHKEGEDRFFPLSGSLIFGKQGTGRDNVDADK420
              || ||| ||: : ||||:|||||| ||||||: |||||| || ||||||| | | ||  :
Db        498 NSNFAWTGAAKFKLNGRDSLMNPGVAMASHKDDEDRFFPSSGVLIFGKQGAGNDGVDYSQ557

Qy        421 VMITNEEEIKTTNPVATESYGQVATNHQSAQAQAQTGWVQNQGILPGMVWQDRDVYLQGP480
              |:||:|||||| ||||||| || || |:|:|  ||||| | |||::|||||:||||||||
Db        558 VLITDEEEIKATNPVATEEYGAVAINNQAANTQAQTGLVHNQGVIPGMVWQNRDVYLQGP617

Qy        481 IWAKIPHTDGNFHPSPLMGGFGMKHPPPQILIKNTPVPADPPTAFNKDKLNSFITQYSTG540
              ||||||||||||||||||:|||||||||||||||||  ||: ||||||||||||
Db        618 IWAKIPHTDGNFHPSPLMGGFGLKHPPPQILIKNTPVPADPPLTFNQAKLNSFITQYSTG677

Qy        541 QVSVEIEWELQKENSKRWNPEIQYTSNYYKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL 599
              |||||||||||||||||||||||||||||||| ||:|||||||||||||||||||||||
Db        678 QVSVEIEWELQKENSKRWNPEIQYTSNYYKSTNVDFAVNTEGVYSEPRPIGTRYLTRNL 736
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Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich/
Primary Examiner, Art Unit 1633